

PRINCIPAL INVESTIGATOR: James N. Kochenderfer, M.D.

STUDY TITLE: Anti-CD30 T Cells with Fully-Human Binding Domains for Treating CD30-expressing Lymphomas including Anaplastic Large Cell Lymphomas

STUDY SITE: NIH Clinical Center

Cohort: Affected Patients

Consent Version: 09/09/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

James Kochenderfer, MD. by phone at 240-760-6062 or Email: kochendj@mail.nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term “you” refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The immune system plays many important roles in the body, such as helping the body fight infections. The immune system is also known to affect cancer cells. “T” lymphocytes, or T cells, are a type of white blood cell and a major part of the immune system. T cells can recognize and destroy many different tumors, particularly types of leukemias or lymphomas. Unfortunately, most tumors have developed ways of escaping the monitoring by the immune system for foreign

or abnormal cells and continue to grow in an uncontrolled manner. We are looking at ways to manipulate the T cells in the immune system, so that they will more efficiently find and kill tumor cells.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You have been diagnosed with a lymphoma (such as: angioimmunoblastic T-cell lymphoma, anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, diffuse large B-cell lymphoma not otherwise specified, primary mediastinal B-cell lymphoma, grey zone lymphoma, enteropathy-associated T-cell lymphoma, or extranodal NK/T-cell lymphoma, nasal type) that has not been controlled by other therapies, meaning that the cancer cells have continued to grow or, if you did achieve a remission, the cancer has recurred after or during treatment. You may have also received an allogeneic transplant because chemotherapy (drug therapy) and/or immunotherapy and/or radiation therapy did not control your cancer growth. For these lymphomas, there are no treatment options that have been proven to cure the cancer. Unfortunately, many lymphomas quickly develop resistance to standard treatment options and ultimately become completely resistant to conventional drug or antibody therapy. Thus, there is a need to find new approaches for the treatment lymphomas. You should discuss with your referring doctor and the NIH doctor's other treatment options that might be available to you so that you feel that you have made the best choice for your disease at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 79 patients will take part in this research study.

DESCRIPTION OF RESEARCH STUDY

What will happen if you take part in this research study?

Before you begin the study

You will need to have the following exams, tests or procedures to find out if you can be in the study. Most of these exams, tests or procedures are part of regular cancer care follow up. However, there are some extra exams, tests and procedures that you will need to have if you take part in this study. If you have had some of them recently, you may not have to do them again.

These tests include:

- Physical examination
- Routine blood and urine tests
- Blood tests for viruses and other disease-causing organisms
- Echocardiogram and EKG of your heart
- Bone marrow biopsy
- CT scan (head, neck, chest, abdomen and pelvis) and/or PET scan
- MRI of your head

During the study

First, you will undergo an apheresis procedure that will remove cells from your blood. Apheresis is a procedure for obtaining certain blood cells, such as white blood cells, without removing most blood cells. It is a process person undergoes when giving routine platelet donations.

Next, we will manipulate your cells in a laboratory so that they can recognize your lymphoma. Specifically, we will genetically modify your T cells and grow them in the laboratory. We hope that these T cells will decrease the amount of cancer you have. However, it is possible that these cells will not have this effect. We will be using a type of virus (lentivirus) that encodes a gene for an anti-CD30 receptor in making these anti-CD30 T cells. Your cancer cells express the CD30 protein on their surface. This CD30 protein will serve as a target for the anti-CD30 T cells.

If it is not possible after 2 attempts to prepare at least enough cells for you to get the number of cells needed by the protocol, you will not be able to be treated on this protocol.

This study is a “dose escalation” study. The purpose of dose escalation is to determine the safe dose of anti-CD30 T cells. There will be five dose levels of anti-CD30 T cells. The first patients enrolled get the smallest dose and the dose is increased when a level has been determined to be safe. You can discuss this with the study doctors to find out which dose of anti-CD30 T cells you will be receiving.

After you have had cells removed from your blood, you will receive two FDA approved drugs (chemotherapy) named cyclophosphamide and fludarabine, over a period of 3 days. The purpose of the chemotherapy is to enhance the activity of the anti-CD30 T cells. You receive a slightly higher amount of cyclophosphamide than some of the first patients on this trial to better enhance this activity. This is a standard chemotherapy regimen that is often used to treat certain types of leukemia. The chemotherapy can be given while you are an outpatient, and a hospital admission is not necessary. It is possible that after you have the cells removed from your blood, your lymphoma may be growing quickly. You may need to receive standard chemotherapy with your oncologist who referred you to this trial, before you can receive the clinical trial therapy. If this happens, you may be able to re-enroll in the study after your lymphoma is better controlled.

Two days after the chemotherapy ends, you will be admitted to the hospital as an inpatient and receive the anti-CD30 T cells. The anti-CD30 T cells are given as a single intravenous (IV) infusion. You will need to have a “central line”, an IV catheter (or tube) placed in a large vein in your arm or chest for this infusion. If you have a catheter in place already, this could possibly be used, or you may need to have an added central line placed. All patients that take part in this study must stay in the hospital for close observation for at least 9 days after the cell infusion, and patients must stay within 60 minutes driving distance for 2 weeks after the cell infusion. This is because in our experience with similar treatments we have noticed side-effects including fevers, fatigue, low blood pressure, and others that have been most severe between



4 and 9 days after cell infusion. You may have to stay in the hospital longer to manage these side effects if they occur.

You will be watched closely during the anti-CD30 T cell infusion for signs of a reaction. While other types of genetically modified T cells have been given to many patients, infusion of anti-CD30 T cells is a new approach that is being studied in this protocol. There is always a chance that we will not be able to genetically-modify your cells or be able to grow the cells in the laboratory. If we are not able to successfully prepare the minimal number of cells that we believe are needed to help control the cancer in our first attempt to produce the cells, we will make a second attempt to produce the cells if you give us permission to do so even if you have already received the chemotherapy part of the protocol at the time. This second attempt to produce cells will probably not be necessary.

When you are finished with the cell infusion

You will need to come for a clinic visit two weeks after your cell infusion, for blood work and a visit with one of our doctors. You will also need to return to clinic for evaluation of your overall health and your lymphoma 1, 2, 3, 4, 6, 9 and 12 months after the cell infusion.

After 12 months, follow up for patients with ongoing responses, which means the lymphoma has not progressed, will continue every 6 months for up to 3 years and then annually after your T-cell infusion. At the follow-up visits we will evaluate your general health, and we will assess your lymphoma. Blood is drawn at all follow-up visits. Note that all these follow-up visits are only needed for patients with ongoing responses.

There is the possibility that you may need to be treated with anti-CD30 CAR T cells a second time if there is still lymphoma left. For you to be treated again, your lymphoma would have had to have some response to the earlier anti-CD30 CAR T-cells. You will only be treated again if the doctors decide it is safe and the treatment may further shrink your lymphoma. There will also need to be enough cells from your first apheresis collection to make the retreatment. We will not be able to re-collect cells. You can be treated up to three times, which consist of your first treatment and two re-treatments. If your lymphoma progresses after you have received your anti-CD30 T-cell infusion(s), you will be removed from the study to start other treatment options. If your lymphoma does not progress, we ask that you do not take any other treatments. We also ask that you do not take any corticosteroid medications such as prednisone or dexamethasone. Corticosteroids and some other medications including chemotherapy will damage the anti-CD30 T cells. They may become less able to fight and get rid of cancer. If you take other treatments or corticosteroids, we can also not tell how well the anti-CD30 T cells are working, and you will be removed from the study. You will be followed by your home oncologist who will receive a detailed summary of your case. They will be told what monitoring tests need to be performed and about possible problems can occur. We encourage early communication of any problems with us so that we can aid in deciding the best treatment approach.



Gene-therapy-specific follow-up

You will be followed on a separate protocol once you are off treatment. Because we do not know the long-term side effects of gene therapy, we will ask you to take part in long term follow up for the next 15 years. The Food and Drug Administration (FDA) requires that people who receive gene therapy be watched even after they complete the study. We will ask you questions about your health and ask you to have a physical exam every year. We will also collect your blood over the next several years. If you return to your referring doctor after treatment here, we will ask you to have your doctor send us a copy of your physical exam and your blood samples. We will collect blood samples right after you receive the cells, and at 3, 6 and 12 months after treatment (2 teaspoons each time). We may also collect your blood over the next several years after 12 months if you have had any previous tests that show a lentivirus in your blood. This testing will help us learn if the cells have grown or changed in your body. For this reason, we ask that you continue to provide us with a current address and telephone number, even after you complete this research study.

At the time of your death, no matter the cause, we may request consent from your family for an autopsy. This will allow us to obtain important information about the safety of this experimental treatment. Please discuss this with your family to inform them of this potential request.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this therapy would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 4 months after you finish the last cell infusion for men, and for 12 months after you finish your last cell infusion for women. If you are a man, you should not donate sperm during the study treatment and for 4 months after you finish the last cell infusion.

If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

TESTS FOR RESEARCH

An important part of this study is testing the effects of this treatment on your tumor and immune system. The following blood samples and tests will be done while you take part in this study:

Research blood samples

Blood will be drawn frequently during your treatment. Most of the blood draws will be to check your health during and after the cell infusion. In addition, some blood samples are drawn for research purposes. Added blood draws might be necessary to investigate T cell responses and serum cytokine levels in cases of clinical events such as rapid regressions of malignancy or toxicity. These samples are to study how your immune system is changed from the cell therapy. Some of the samples may be used for other or future research conducted by the investigational team or other researchers inside and/or outside of NCI or the NIH. In general, 4 tablespoons will be drawn at each clinic visit or every Monday, Wednesday, and Friday during the inpatient stay. There will also be about a 1 tablespoon draw the day you receive the cells and the first Sunday afterwards. On one occasion before the treatment a larger amount of blood (8 tablespoons) will be drawn. The NIH has set a limit on the largest amount of blood that can be taken for research. This limit is based on your age. For adults, no more than 37 tablespoons can be taken over an 8- week period.

Lumbar Puncture

If you have a form of lymphoma that has a tendency to spread to the lining of the brain or spinal cord (called the leptomeninges) or if there is any concern that this might have occurred, you may also require a lumbar puncture to determine whether you would require special therapy that should not be delayed while participating on an experimental protocol. The procedure uses local anesthesia to numb the skin in the lower back, and a very thin needle draws fluid from the area below the spinal cord. Approximately one-to-three teaspoons of the fluid that bathes the spinal cord (called the cerebrospinal fluid) would be removed and examined for tumor cells.

Bone Marrow Biopsies

A bone marrow biopsy is performed before the start of treatment. You may need to have added bone marrow biopsies during the study if there is lymphoma in your bone marrow before you start the study and if you are in remission after your anti-CD30 T cell infusion. These bone marrow biopsies are performed to make sure there is also no cancer in your bone marrow. These biopsies are needed for participation on the study to evaluate your tumor but also for research tests.

Tumor Sampling

Before or at the end of cell therapy, we may ask your permission to perform a biopsy of your cancer. If we can safely perform a biopsy without general anesthesia or significant risk of danger or discomfort to you, a sample may be removed through a surgical procedure or with a needle biopsy. A surgeon will go over the details before the procedure and will ask you to sign a separate consent. The primary risks are pain from the needle insertion and a slight risk of infection, bleeding, or injury to the nearby tissue. Biopsies are performed under sterile conditions to prevent infections. We may also ask your permission to perform a biopsy for research. The tissue from this biopsy is used to see how the CAR T cells are affecting the tumor or to see if a new tumor is lymphoma. Any biopsies would only be performed with your permission. The biopsy also has to be determined safe by the Principle Investigator of this trial

and the physician or physicians that would perform the biopsy. Some of the samples may be used for other or future research studies by the investigational team or other researchers. This future research might directly study malignancy of the same type that you have, or it could focus on other areas of research.

CT SCAN

You may have a CT (Computed Tomography) scan of areas as needed for disease assessment) at 1-month, 2-month, 3-month, 4-month, 6-month, 9-month and 12 months after T cell infusion. This may include areas such as the neck, chest, abdomen and pelvis. If is necessary, we may use contrast agent enhanced CT scans. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes.

PET SCAN

You may have PET (Positron Emission Tomography) scan at 1-month, 2-month, 3-month, 4-month, 6-month, 9-month and 12-months if needed to stage disease. The PET scanner is a doughnut-shaped machine that uses x-rays combined with a dose of a radioactive substance (tracer) to create computer pictures showing the inside of your body.

Before the scan, you will have a radioactive substance injected into your arm after which, you will need to wait for approximately 30 minutes for the substance to be absorbed. After 30 minutes, you'll lie on a narrow, padded table and be positioned for the scan. The scan itself is painless and won't make much noise. During this time, you will need to lie very still. It will take about another 30 minutes to complete.

RISKS OR DISCOMFORTS OF PARTICIPATION

Because the CD30 protein is on normal B and T cells (types of white blood cells or immune cells) as well as on your cancer, the anti-CD30 T cells might cause a fleeting or prolonged decrease in the number of normal B and T cells. Because B and T cells are involved in protection against infections, this decrease in B and T cell number might lead to a greater risk of infections. We do not know if a decrease in normal B and T cells will cause problems with infections. We take steps to deal with the increased risk of infection or actual infections.

The anti-CD30 T cells we will be giving you have been changed to express the anti-CD30 part that targets the T cells to the cancer by using a virus (retrovirus). Although this retrovirus is not active, there is the rare possibility that it may cause infection. The cells could also cause you to develop another type of cancer in your blood cells, although we think this is very unlikely. Other gene-modified T cells have been given to hundreds of individuals before, and in no patient receiving T-cell gene therapy has an infection or cancer developed that was shown to be caused by the retrovirus used.

Some patients died on different studies that used CAR T cells that use a different target, called CD19, which is on some lymphomas and leukemias. Several other patients have been treated with anti-CD19 CAR T cells without major adverse effects. Many patients receiving anti-

CD19 CAR T cells at many hospitals have developed fever and fatigue that can last for up to 2 weeks after cell infusion. Some patients that have received similar treatments have developed low blood pressure. A small number of patients developed a temporary decrease in heart function after being treated on similar study at this institute. Their heart function later returned to normal levels and the other participants in the study have not had decreased heart function. One patient on an anti-CD19 CAR T-cell study had tumor lysis syndrome, which is a release of toxins from destroyed tumor cells. This tumor lysis syndrome was treated and caused no long-term problems for the patient. Patients at risk of tumor lysis syndrome will receive medication to prevent this complication. Neurological toxicities such as a temporary loss of the ability to speak, temporary confusion, and temporary difficulty walking have occurred in several patients.

Some laboratory testing suggests that CD30 is present in a woman's uterus during pregnancy and certain parts of the menstrual cycle. It is possible that the anti-CD30 T cells could damage the uterus, or the unborn baby in pregnant women. For this and other reasons, pregnant women and women having menstrual periods should not participate in the trial.

Potential risks of anti-CD 30 T cells infusion include:

<u>Likely:</u>	<u>Less Likely:</u>	<u>Rare:</u>
<ul style="list-style-type: none"> • Fever • Chills • Shortness of breath (these side effects may last a few hours) • Fatigue • Somnolence (excessive sleeping) • Low antibody levels which might need antibody replacement infusions • Infections caused by immunosuppression • Mild rash 	<ul style="list-style-type: none"> • Headache • General feeling of being unwell (malaise) • Lung congestion • Severe rash • Itching • Cytokine Release Syndrome (release of substances from T cells that can cause many side-effects) including <ul style="list-style-type: none"> ○ Fever ○ Fast heart rate ○ Low Blood Pressure ○ Possible intensive care unit admission ○ Mechanical ventilation ○ Rare cases, death. 	<ul style="list-style-type: none"> • Death • Permanent kidney damage • Coma • Permanent neurologic impairment

<u>Likely:</u>	<u>Less Likely:</u>	<u>Rare:</u>
	<ul style="list-style-type: none"> • Low blood pressure • Tumor lysis syndrome (rapid breakdown of tumor that can cause side-effects) <ul style="list-style-type: none"> ○ Possible intensive care unit admission ○ Fast heart rate ○ Possible kidney damage that will most likely be temporary ○ Possible breathing problems that might in rare cases need mechanical ventilation (breathing machine) • Temporary decreased cardiac function • Temporary liver function test elevation • Temporary decrease in blood counts (may last up to few weeks) 	

<u>Likely:</u>	<u>Less Likely:</u>	<u>Rare:</u>
	<ul style="list-style-type: none"> • Temporary low calcium, phosphorous, albumin in the blood • Muscle inflammation and pain • Increase in bleeding times • Temporary neurological changes, ex: confusion, difficulty speaking, decreased balance, seizures, tremor (shaking) of hands, poor balance • Graft versus Host Disease (GVHD) possible ONLY if you have had an allogeneic stem cell transplant • Damage to a woman's uterus • Fainting 	

As this is a new experimental therapy, new unexpected side effects may happen and cause your condition to worsen.

Potential risks of Cyclophosphamide:

Likely:	Less Likely:	Rare:
<ul style="list-style-type: none"> • Low blood counts 	<ul style="list-style-type: none"> • Nausea and vomiting • Painful and bloody urination • Sterility • Water retention • Hair loss 	<ul style="list-style-type: none"> • Heart damage • Secondary leukemia (a different type of cancer) • Skin rash • Bleeding

Potential risks of Fludarabine:

Likely:	Less Likely:	Rare:
<ul style="list-style-type: none"> • Low blood counts 	<ul style="list-style-type: none"> • Long-term reduction of lymphocyte counts which could increase the risk of infection • Infection 	<ul style="list-style-type: none"> • Seizures, coma, blindness and even death • Inflammation in the lungs • Kidney damage

Gene Therapy Risk of Cancer and Other Diseases

We are unsure if this type of gene therapy will cause you to become sick in the future. It is possible that it may cause your immune system or nerves not to work well or cause a sickness of your blood cells or even a cancer (for example leukemia). We do not know if you will develop any of these disorders, but you need to be aware of this possible risk. Children in France and England received gene therapy for a disease of the immune system. Most of the children were cured but 5 children out of 20 later developed leukemia and one died. Experts who looked at these cases thought that the gene therapy caused the leukemia in these children. Because you will be receiving a gene therapy that is very different from the gene therapy that these children received, the chance of this therapy causing a second cancer may be lower. In fact, hundreds of patients have received T-cell gene therapies like the one that you will receive without any of them developing a cancer that caused by the T-cell gene therapy. To watch you for this risk we will be testing your blood as described before.

Graft-Versus-Host Disease (GVHD):

This is only for patients that have previously received an allogeneic transplant only. Early (acute) GVHD, which generally occurs in the first 100 days after transplantation and sometimes occurs after donor lymphocyte infusion, may occur following infusion of the anti-CD30 T cells. Mild acute GVHD (skin rash only) is treated with topical steroid lotions. More severe acute GVHD can cause blistering of the skin, abdominal pain and diarrhea, disturbances in liver function and jaundice and needs strong treatment including steroids, which are given intravenously (through the vein). Occasionally, severe acute GVHD can be fatal. Delayed or chronic GVHD may also occur. Typically occurring after the first 100 days following transplantation, it also can occur after donor lymphocyte infusion, and may occur after anti-CD30 T cell therapy. Symptoms include dryness of the mouth and eyes, skin rash, joint stiffness, weight loss, liver damage (including jaundice), and lung damage leading to cough

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

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and shortness of breath. This is treated with drugs that suppress the immune system, such as cyclosporine and steroids given by mouth. Chronic GVHD can at times be present for the rest of your life. Both acute and chronic GVHD, and the drugs we use to treat them, can place patients at significant risk for infections, which can be life-threatening. **Blood Draws:**

Blood will be drawn often during your treatment. Most of the blood draws will be to watch your health during and after the lymphocyte infusion. In addition, some blood samples will be drawn for research purposes. Added blood draws might be necessary to investigate T cell responses and serum cytokine levels in cases of clinical events such as rapid regressions of malignancy or toxicity. These samples will be used to study how your immune system is affected by the cell therapy, a graft-versus-tumor response and graft-versus-host disease (if it occurs). Some of the samples may be used for other or future research conducted by the investigational team or other researchers. In general, 20 to 70 ml of blood (4 to 12 teaspoons) will be drawn at each clinic visit or inpatient hospital day. Side effects of repeated blood sampling depend in part on how the blood is drawn. If through a central venous catheter, you risk the catheter. This can cause a serious blood stream infection that requires admission to the hospital to give you antibiotics through the vein. If blood is drawn through a needle into your skin, side-effects could include pain and bruising in the area where the blood was drawn. Other side-effects can include lightheadedness, or rarely, fainting. If you have too much blood taken over a prolonged period, your red blood cell count may drop (this is called "anemia"). As a precaution, we will check your red blood cell level, and give you iron treatment or a blood transfusion if needed.

Intravenous Catheter:

In order to receive this treatment, you will need to have a central venous catheter. This catheter is placed under the skin of the arm and threaded to a major vein in the chest. There are several types of catheters including those which must be removed after each treatment (temporary type) and those which may be kept longer (permanent type). These options will be discussed with you. The risks associated with placing some catheters include pain, bleeding, infection and collapsed lung. The long-term risks of the catheter include infection and clotting of your veins. If these occur, it may be necessary to remove the catheter. These risks will be explained to you in more detail at the time of insertion.

Bone marrow aspiration and biopsy:

A bone marrow biopsy is performed by inserting a needle into a bone of the hip. In the aspiration part of the procedure, a small amount of liquid bone marrow is removed, and in the biopsy part, a tiny solid piece of bone marrow is removed. You may feel a pressure sensation when the needle is being inserted and a pulling sensation and brief pain as the marrow is withdrawn. The amount of marrow taken is very small and will not change your body's ability to form blood cells. Potential complications of this procedure are local bleeding, pain at the site, and infection. Both are very rare. Bleeding can be stopped by applying local pressure and an infection can be treated with antibiotics.

Lumbar Puncture:

There is very minor discomfort when the numbing medicine is injected into the skin. It may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. A third or fewer patients may experience some headache while the body replaces the fluid that is removed.

Apheresis:

The risks of apheresis are similar to whole blood donation and include pain and bruising at the needle insertion site in the arms, lightheadedness, dizziness, nausea, and rarely fainting due to a rare reflex reaction to needle placement and to the temporary decrease in blood volume during apheresis. You may also feel tingling around your mouth or in your fingers caused by a blood thinner given during the procedure. The nurses will give you a calcium containing antacid to chew to reduce the tingling. All the symptoms usually go away within a few minutes of stopping the procedure. We ask that you eat a meal before coming to donate, and avoid caffeine, to prevent lightheadedness or dizziness that might occur. You will be asked to remain in the chair/bed for a few minutes after the donation is completed, and to sit down and relax for about 15 minutes after the donation. This is done so that staff can observe you to make sure that you feel entirely well before you leave our department.

Optional Biopsies:

You may be asked to undergo a biopsy for research purposes. Tumor biopsies can be performed as an outpatient surgical procedure or can be done by a specialist using the CT scanner or ultrasound machine to guide the biopsy needle into the tumor to ensure accuracy. There are risks associated with the biopsies, which can include pain and bleeding at the biopsy site. The biopsies to be performed are exclusively for research purposes and will not benefit you. It might help other people in the future. You will be asked at the time of the procedure if you are willing to have this biopsy.

What are the risks of radiation from being in the study?

During your participation in this research study, you may be exposed to radiation from CT scans of your neck, chest, abdomen and pelvis, CT guided biopsies and 18FDG-PET/CT scans each year. The amount of radiation exposure you will receive from these procedures is equal to approximately 22.4 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called “background radiation.” This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans and 18FDG-PET/CT scans that you get in this study will expose you to the roughly the same amount of radiation as 74.7 years’ worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100

people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 2.2 out of 100 (2.2%) and of getting a fatal cancer is 1.1 out of 100 (1.1%).

If you can become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time

Contrast Agent enhanced CT scans risks:

If contrast dye is used, there is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems. The study doctors will do a blood test prior to the test to confirm that it is safe you to receive the contrast.

For IV contrast if used: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

For oral contrast if used: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after drinking the contrast.

POTENTIAL BENEFITS OF PARTICIPATION**Are there benefits to taking part in this study?**

It is unknown at this time whether anti-CD30 T cell infusions will improve survival or have any benefit for patients with lymphomas. If accepted by your body, the cell infusion may decrease the amount of your cancer. Your participation in this experimental treatment may also help us advance the understanding and treatment of lymphomas with T-cell therapies, so your participation could help other patients. We do not know if you will receive personal medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer .

ALTERNATIVE APPROACHES OR TREATMENTS**What other choices do I have if I do not take part in this study?**

To be eligible for this protocol, you may or may not have already received an allogeneic HSCT. Prior to this, you have received some of the conventional therapies for your disease. Before deciding whether to participate in this clinical trial, you may consider other treatments such as:

- Other forms of chemotherapy, radiation, surgery, or immune therapies, without being in a study.
- You may be eligible for other experimental therapies.
- Another option is not to receive any further therapy at all, other than comfort care, also called palliative care. This type of care reduces tiredness, appetite problems and

other problems caused by the cancer. It does not treat cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

You should discuss with your referring doctor and the NIH doctors whether any of these treatments might represent a reasonable treatment option for your disease.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment (you may also be eligible for a second infusion of the anti-CD30 T cells if this happens)
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if you become pregnant
- if the study doctor decides to end the study

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Dr. Kochenderfer or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases **cannot** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines, but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to \$15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.



USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.



- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY**Will your medical information be kept private?**

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor or his agent(s)

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.



The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Jim Kochenderfer, M.D., Building 10, Room 12C121, Telephone: 240-760-6062. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.



Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant

Print Name of Research Participant

Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR

Print Name of LAR

Date

Investigator:

Signature of Investigator

Print Name of Investigator

Date

Witness to the oral short-form consent process only:

Witness:

Signature of Witness*

Print Name of Witness

Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.